Stem Cell Mechanisms Governing Discrete Waves of Gliogenesis in the Childhood Brain

Grant Award Details

Stem Cell Mechanisms Governing Discrete Waves of Gliogenesis in the Childhood Brain

Grant Type: Basic Biology IV

Grant Number: RB4-06093

Project Objective: The proposed experiments seek to define cellular and molecular mechanisms governing neural stem and precursor cell differentiation into functional myelinating oligodendrocytes during the protracted and vulnerable period of postnatal brain maturation that spans the first three decades of human life.
Aims are to: evaluate the spatiotemporal distribution of glial progenitor cells (OPCs) and postnatal gliogenesis; examine neuronal instruction of postnatal gliogenesis; and test contributions of reciprocal Hedgehog-Wnt signaling to mid-childhood pontine gliogenesis.

Investigator:

Name:	Michelle Monje
Institution:	Stanford University
Type:	PI

Disease Focus: Neurological Disorders, Pediatrics

Human Stem Cell Use: Adult Stem Cell, Embryonic Stem Cell

Award Value: $1,264,248

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Grant Application Details

Application Title: Stem Cell Mechanisms Governing Discrete Waves of Gliogenesis in the Childhood Brain

Public Abstract: White matter is the infrastructure of the brain, providing conduits for communication between neural regions. White matter continues to mature from birth until early adulthood, particularly in regions of brain critical for higher cognitive functions. However, the precise timing of white matter maturation in the various neural circuits is not well described, and the mechanisms controlling white matter developmental/maturation are poorly understood. White matter is conceptually like wires and their insulating sheath is a substance called myelin. It is clear that neural stem and precursor cells contribute significantly to white matter maturation by forming the cells that generate myelin. In the proposed experiments, we will map the precise timing of myelination in the human brain and changes in the populations of neural precursor cells that generate myelin from birth to adulthood and define mechanisms that govern the process of white matter maturation. The resulting findings about how white matter develops may provide insights for white matter regeneration to aid in therapy for diseases such as cerebral palsy, multiple sclerosis and chemotherapy-induced cognitive dysfunction.

Statement of Benefit to California: Diseases of white matter account for significant neurological morbidity in both children and adults in California. Understanding the cellular and molecular mechanisms that govern white matter development the may unlock clues to the regenerative potential of endogeneous stem and precursor cells in the childhood and adult brain. Although the brain continues robust white matter development throughout childhood, adolescence and young adulthood, relatively little is known about the mechanisms that orchestrate proliferation, differentiation and functional maturation of neural stem and precursor cells to generate myelin-forming oligodendrocytes during postnatal brain development. In the present proposal, we will define how white matter precursor cell populations vary with age throughout the brain and determine if and how neuronal activity instructs neural stem and precursor cell contributions to human white matter myelin maturation.

Disruption of white matter myelination is implicated in a range of neurological diseases, including cerebral palsy, multiple sclerosis, cognitive dysfunction from chemotherapy exposure, attention deficit and hyperactivity disorder (ADHD) and even psychiatric diseases such as schizophrenia. The results of these studies have the potential to elucidate clues to white matter regeneration that may benefit hundreds of thousands of Californians.